Guidelines for Treatment Regimens

EXPRESSION AND NOMENCLATURE

September 19, 1997

INTRODUCTION

All protocols sponsored by the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI), are reviewed for safety and scientific integrity. Cancer Therapy Evaluation Program (CTEP) staff have developed standardized guidelines to express chemotherapy regimens in a uniform, clear and consistent manner. The intention of the guidelines is to minimize undue risks to patients on DCTD sponsored investigational clinical trials. **DCTD-sponsored protocols will not be approved unless they comply with the *Guidelines for Treatment Regimen Expression and Nomenclature***. CTEP will screen all protocol related documents to assure compliance with the treatment regimen guidelines. These guidelines should be used in all facets of protocol development including Letters of Intent (LOIs), Concept Reviews, protocols, protocol amendments, protocol related publications and any other protocol related correspondence.

The development and utilization of a clear and consistent method for expressing chemotherapy dosage schedules and treatment regimens is an important public health issue. Recent events have heightened awareness and concern among medical professionals and the general public to the potential for adverse and fatal outcomes as a consequence of medication errors with oncology agents. The American Society of Health-System Pharmacists (ASHP), the American Medical Association (AMA), and the American Nursing Association (ANA) have recommended systematic standardized approaches to reducing medication errors, which include educating health care providers and patients regarding appropriate drug therapy, improved collaboration between health care providers, establishing dosage limits, and standardizing a prescribing vocabulary. The *Guidelines for Treatment Regimen Expression and Nomenclature* are intended to supplement and reinforce the AMA, ANA, and ASHP recommendations with specific examples illustrating how the guidelines can be applied during protocol development.

Comments and recommendations regarding the treatment regimen guidelines were solicited from clinical pharmacists from comprehensive cancer centers, home infusion services, industry and the Cooperative Group pharmacy chair. Guidelines for expressing dose regimens in treatment plans, drug orders, physician notes and product labeling have also been developed. Investigators should refer to *Standardized Guidelines for Treatment Regimens Expression and Nomenclature*, ASHP 1997, for additional information on this topic.

POLICY

Instructions for dose regimens should be complete, clear, and simple to follow. Treatment regimens should be expressed accurately, completely and consistently throughout a protocol document.

GENERAL GUIDELINES

- **Do not abbreviate** drug names or treatment schedules. Abbreviations can be misinterpreted.
- Use complete approved **generic drug names**. Brand names and abbreviations are not acceptable (e.g., specify 'carboplatin' instead of CBDCA, 'cisplatin' instead of CDDP).
- **Treatment instructions should be explicit**. No detail (no matter how minor) should be omitted; however, avoid unnecessary redundancy.
- **Delete extraneous information** that may confuse readers (e.g., protocols that use only injectable drugs products should not include information for a tablet formulation).
- **Use consistent notation** in expressing quantifiable units, (ex. either; 1mcg or 1ug or 1mg; qid or Q6h; kg or m2)
- **The word, "Units"** should be spelled out to avoid confusion; a letter "U" can be easily mistaken for a zero and may result in a 10-fold overdose.
- Decimal Points -
    - Never trail a whole number with a decimal point followed by a zero (i.e., "5 mg" not "5.0 mg"). The decimal point may not be seen, resulting in a 10-fold overdose. •In expressing units that are less than the whole number one, the dosage should be written with a decimal point preceded by a zero (i.e., ".125 mg" not "0.125 mg"). Without the 'zero' prefix, the decimal point may be missed resulting in a dosing error.
- **Body weight** - Drug dosages may be expressed as a function of body surface area, body weight, or may be calculated to produce a pharmacokinetically-targeted endpoint (e.g., serum or plasma concentration or area under the curve [AUC]). Treatment plans should specify whether absolute (i.e., actual), ideal, or lean body weight is used in calculating drug dosage as a function of body weight. In addition, an equation describing how that value is calculated should appear in the treatment plan if drug dosage is a function of a calculated ideal or lean body weight. If drug dosage is a function of a calculated pharmacokinetic endpoint, the equation(s) describing how that value is calculated should also appear in the treatment plan.
- **Contiguous treatment days** - Treatment plans should specify the total number of days a drug is administered and the cycle day that treatment commences. Include parenthetically the cycle days on which treatment occurs.
- **Non-contiguous days** - Treatment plans should specify the cycle days on which each dose should be given.
- **Cycle (or Course) duration** - Treatment cycle duration (or length) should be specified. When a treatment regimen is 21 days in duration, the regimen will be repeated on the twenty-second, forty-third, sixty-fourth…, etc. days following treatment initiation.
- **Duration of administration**:
    - Administration duration should be clearly indicated. If a drug is to be administered on more than one day per cycle, each cycle day should be explicitly identified.
    - "Day One" typically describes the day on which treatment commences when treatment day enumeration is arbitrary. Avoid using *'day 0 (zero)'* when describing treatment schedules unless it is necessary (*e.g*., when describing the day on which hematopoietic progenitor cells are administered after a cytotoxic conditioning regimen in transplantation protocols).

- **Clarify total dose planned per treatment course** - In all treatment plans (protocols) and drug orders, identify and append parenthetically the total dose (as a function of body weight or surface area) that patients are to receive during a treatment course (or cycle).
- **Administration Dates and Times** - When appropriate include specific starting days and times. Directions indicating events for the twelve o'clock hours should be explicitly expressed (spell out) "12:00 noon" and "12:00 midnight." Expressing time by 24-hour clock notation ('military time') likewise precludes errors due to ambiguous 'a.m.' and 'p.m.' time notations.

- **Treatment information should contain the following elements:**

	drug name	**dosage**	**administration vehicle name and volume**	**administration route**	**administration instructions**
example 1	ABC	200 mg/m2	0.9% sodium chloride injection 500 mL	intravenously	over 1 hour
example 2	XYZ	50 mg/m2	n/a	orally	with food

	administration schedule	**number of doses to administer, treatment duration, or date when treatment should be discontinued**	**starting dates (and times when appropriate)**	**total amount of drug administered per course (expressed parenthetically)**
example 1	every 12 hours	for 6 doses	start on day 1	(total dose/cycle = 1,200 mg/m2)
example 2	every morning	for 14 days	start on day 1	(total dose/cycle = 700 mg/m2)

PARENTERAL ADMINISTRATION

- Drug products should be prepared within documented stability and sterility guidelines in accordance with practitioners' local clinical and institutional policies and procedures. Drug containers should be changed at least daily unless extended stability and sterility data are available.
- In protocol descriptions and orders for treatment, drug dosage should be expressed as the total amount of drug that will be administered from a single drug container, i.e., the total amount of drug per syringe, bag, or other container that will be dispensed. An exception to this rule applies to drug products with extended stability, where a drug is administered from a single container for greater than 24 hours. In such cases, treatment plans and prescribers' orders should specify the amount of drug that is administered during each 24-hour interval. Product container labels should always identify the amount of drug within the container.
- For drug admixtures that can be prepared in more than one way, practitioners should institute a priori, standard and consistent methods governing how each drug will be prepared and administered.
- Include specific fluid volumes and types when possible.

EXAMPLES

Bolus infusion (administration duration ≤ 24 hours):

- Express the amount of drug per container.
- Include the rate of administration, the infusion duration, and days on which the drug is to be administered.

example

"XYZ" 15 mg/m2 diluted in 50 mL 0.9% sodium chloride injection, infuse intravenously over 15 minutes for one dose on day 1 (total dose/cycle = 15 mg/m2)

Drug products stable for ≥ 24 hours - (Containers are prepared daily):

- Express the dose per container.
- Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses.
- State that the agent must be prepared daily.

example

"XYZ" 8 mg/m2 per day diluted in 50 mL 0.9% sodium chloride injection, administer by continuous intravenous infusion over 24 hours, daily for three days starting on day 1 (days 1, 2, and 3; total dose/cycle = 24 mg/m2 over 72 hours). A new IV bag should be prepared daily for 3 days.

Drug products stable for ≥ 24 hours - (Containers are prepared for multiple days):

- Express the dose as the amount of drug administered per day and indicate the number of days for which it is administered.
- Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses.
- State that this is a multi-day preparation and for how long the preparation should be infused.

example

"XYZ" 8 mg/m2 per day diluted in 50 mL 0.9% sodium chloride injection, by continuous intravenous infusion for three days starting on day 1 (total dose = 24 mg/m2 over 72 hours). This is a multi-day infusion to be infused over 72 hours.

Continuous infusions that require multiple drug product containers:

- Express the dose per container.
- Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses.
- Include the total number of containers used per day.

example

"XYZ" 1 mg/m2 diluted in 50 mL 0.9% sodium chloride injection, administer by continuous intravenous infusion over three hours, every three hours for three days, starting on day 1 (8 bags/day, total dose = 24 mg/m2 over 3 days)

ORAL ADMINISTRATION

- Describe drug dosages and schedules as the amount of drug that will be given (or taken) each time the drug is administered, not as a total daily dose that will be given (or taken) in divided doses, (e.g. 20 mg orally every 6 hours for 5 days vs. 80 mg per day, given in four divided doses for 5days
- Include guidelines regarding 'rounding-off' doses to the nearest capsule or tablet size. Although breaking a tablet into halves at best approximates an accurately measured dose, treatment plan rounding-off rules should indicate whether tablet formulations should be broken to deliver a calculated dosage.
- Whenever possible, include instructions about whether drugs should be administered (or taken) with food and any dietary restrictions.

CONCOMITANT (ANCILLARY) MEDICATIONS

- Supportive care and essential ancillary medications required by a treatment regimen should be clearly identified.
- Complete instructions including appropriate indication, dosage, administration route, schedule, restrictions to use, and any other relevant data should be explicitly stated.

- Treatment plans should explicitly identify when treatment (typically dosage) modifications are appropriate.
- Treatment modifications and the factors predicating treatment modification should be explicit and clear.
- All treatment modifications should be expressed as a specific dose rather than as a percent of the starting dose.